

**UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY**

ASTRAZENECA AB, AKTIEBOLAGET
HÄSSLE, ASTRAZENECA LP, KBI INC.
and KBI-E INC.,

Plaintiffs and
Counterclaim-Defendants,
v.

HANMI USA, INC., HANMI
PHARMACEUTICAL CO., LTD., HANMI
FINE CHEMICAL CO., LTD. and HANMI
HOLDINGS CO., LTD.,

Defendants and
Counterclaim-Plaintiffs.

Civil Action No. 3:11-CV-00760-JAP-TJB

Judge Joel A. Pisano
Magistrate Judge Tonianne J. Bongiovanni

DECLARATION OF DR. DAVID A. JOHNSON ON CLAIM CONSTRUCTION

I, David A. Johnson, MD hereby declare:

I. EDUCATIONAL BACKGROUND AND QUALIFICATIONS

1. I am a Professor of Medicine and Chief of Gastroenterology at the Eastern Virginia School of Medicine in Norfolk VA.

2. I am boarded in gastroenterology and internal medicine. I have been active in the field of gastroenterology for over twenty-eight years. This involvement has included extensive contributions to the literature with over 600 articles, book chapters and abstracts published. I have given hundreds of invited lectures throughout the world and been a regular participant in national and international educational meetings with a particular focus and interest and expertise in esophageal and colon disease.

3. I currently serve as co-editor of the American College of Gastroenterology Education Universe; esophageal section editor for the *New England Journal of Medicine*; Journal Watch Gastroenterology; GI editor Medscape (WebMD); GI editor Medscape Computer GI Consult; and Medscape GI Viewpoints. Additionally, I have served on the editorial board as Associate editor for the *American Journal of Gastroenterology* from 1988 through 2004 as well as the editorial boards for *Digestive Diseases and Gastrointestinal Endoscopy*. I am an active reviewer for eleven medical journals at present. I have also served as co-editor for the American College of Physicians Book “*Dyspepsia*” as well as Gastroenterologic Clinic of North America, “*Obesity Related Issues for the Gastroenterologist*” published in 2005 and again as a new issue update in 2010.

4. I was recently selected by the American Board of Internal Medicine to serve on the Gastroenterology Subspecialty Examination Committee. In this capacity, I will help oversee

evaluation of all U.S. based physicians who seek board certification and re-certification in gastroenterology.

5. My curriculum vitae is attached as Exhibit A.

6. I have had extensive involvement with clinical research for my entire career. I continue to play a very active role in that area. This involvement includes generation of protocols, as well as participation in phase 1, 2, 3 and 4 studies, many of which have been pivotal studies leading to FDA approval of the medication or device being studied. I have been the primary presenter for a large number of these studies at national and international presentations. I have additionally served as a presenter to the FDA advisory panel.

7. Throughout my entire career, I have held numerous consultant and advisory positions. These have included positions at the National Cancer Institute, Centers for Medicare and Medicaid(CMS), GI advisor for National Quality Forum, as consulting gastroenterology attending physician to Congress, as well as for a number of pharmaceutical advisory boards and national and international expert consensus panels. These expert consensus panels have included particular focus on evidence-based medicine and gastroesophageal reflux disease (“GERD”). I was an invited participant for the 2005 International Global Consensus Working Group on GERD, which involves approximately thirty invited world experts on reflux disease. I have also served as an active advisor and reviewer for the 2005 American College of Gastroenterology National Guidelines for Management of gastroesophageal reflux disease.

8. As set forth in my curriculum vitae, I have been extensively involved in leadership positions both for state and national associations and societies. I have had an active role with Medicare, co-chairing the national GI Medicare Carrier advisory committee for nine years and serving as the Virginia State representative for that same tenure. I have previously

served as the GI Specialty Advisor for the State of Virginia for Anthem Blue Cross Blue Shield. I served on the American College of Gastroenterology Board of Trustees from 1995-2008 and was President from 2006-2007 and am on the executive committee and current Treasurer of the ACG/ASGE Quality Improvement Consortium National Registry project. In these positions, I have served not only in guiding policy but also helping to establish standards of best care and best practice for patients. In fact, working with State Senator Emily Couric in 2004, I was the physician responsible for developing the colon cancer screening bill for the State of Virginia. In this capacity I spent approximately two years working with Senator Couric in making presentations to a number of state legislative committees, meeting with the Governor, all ultimately leading to successful passage of a colon cancer screening benefit for citizens of Virginia. This represented the first such bill of its kind and set a standard for states which are currently pursuing similar legislation.

9. Despite a larger commitment to leadership in state and national societies as well as my participation in educational activities and contributions to the literature, my primary focus is patient care. On a daily basis in my practice I see both hospital and office patients. As such, I feel particularly qualified to speak to standards of care, best practice strategy and what patients and physicians consider significant and meaningful care strategies and outcomes.

II. SCOPE OF DECLARATION

10. I understand that this litigation involves AstraZeneca patents 5,714,504 (the “’504” patent) and 5,877,192 (the “’192” patent), which claim salts of the (–)-enantiomer of omeprazole, formulations containing those salts and methods of treatment using these salts and the non-salt form of the (–)-enantiomer of omeprazole.

11. I am aware that AstraZeneca markets the magnesium salt of the (–)-enantiomer of omeprazole as Nexium®. The active ingredient of Nexium® (the magnesium salt of the (–)-enantiomer of omeprazole) is also known as esomeprazole magnesium.

12. I understand that Hanmi has applied for permission from the U.S. Food and Drug Administration to sell a version of Nexium® prior to the expiration of the '504 and '192 patents. I also understand that AstraZeneca sued Hanmi for infringement of the '504 and '192 patents.

13. I have been asked by counsel for AstraZeneca to provide my opinion on the knowledge and understanding of a person of ordinary skill in the art, and the understanding such a person would have of the following terms from the claims of the '504" patent:

- “administration of” and “administration to;”
- “a mammal including man in need of such treatment;”

and the '192 patent:

- “administering to a mammal in need of treatment.”

14. Counsel for AstraZeneca has provided me with the following documents, which I have reviewed and considered in providing my opinions stated herein:

- the '504 patent and its prosecution history;
- the '192 patent and its prosecution history;
- parent applications and prosecution histories to the '504 and '192 patents including U.S. Application 08/256,174, WO 94/27988 and SE 9301830;
- the Parties Joint Claim Construction and Prehearing Statement including Exhibits A through D; and
- the Nexium® Product Label.

15. I have not testified as an expert at trial or by deposition during the past four years. I am being paid five-hundred dollars per hour for my time spent in study and testimony in this matter.

16. I reserve the right to prepare exhibits to summarize or support the opinions set forth below.

III. SCIENTIFIC BACKGROUND

17. Should the court determine that it would be helpful, I am prepared to provide a tutorial on scientific and medical aspects of the gastrointestinal system; gastrointestinal diseases, including acid-related gastrointestinal disease and gastrointestinal inflammatory disease; and protein pump inhibitors (“PPIs”), including Nexium®, and their therapeutic applications and usage.

IV. OPINIONS

A. The Person of Ordinary Skill in the Art

18. Counsel has informed me that the claims of a patent define the scope of rights under the patent. Patents typically include several claims, and the claims are intended to define the invention by one or more of its characteristics. Different aspects of the invention can be defined in different claims. A claim that makes reference to an earlier claim must be read as a definition of an aspect of the invention that includes the definition in the earlier claim, and adds to it, or further limits it.

19. Counsel has informed me that only certain claims of the ’504 and ’192 patents are at issue in this litigation. The asserted claims of the ’504 patent (claims 1–7 and 10) are generally directed to “pharmaceutical formulation[s]” containing an “alkaline salt” of (–)-omeprazole and methods of use thereof for “inhibiting gastric acid secretion” and “treatment of gastrointestinal inflammatory disease.” The asserted claims of the ’192 patent (1–7, 10–19 and 21–23) are generally directed to methods for the “treatment of gastric acid related diseases” with

(-)-omeprazole “or a pharmaceutically acceptable salt thereof” and to methods for the “production of a medicament for treating gastric acid related diseases” containing the same.

20. I have been instructed by counsel for AstraZeneca that the court determines the meaning of claim terms in a judicial process known as claim construction. I understand that the claims of a patent must be read from the viewpoint of a hypothetical person of ordinary skill in the art. As mentioned above, I have been asked to address claim terms that pertain to concepts of pharmaceutical administration and treatment of patients with diseases or disorders of the upper gastrointestinal tract. In my opinion, a hypothetical person of ordinary skill in the art would have skills in both chemistry and in treating disorders of the upper gastrointestinal tract. The skills in treating disorders of the upper gastrointestinal tract of a hypothetical person of ordinary skill in the art would in my opinion require at least an M.D. degree, post-graduate training in medicine, a fellowship in gastroenterology and experience in treating any number of diseases or disorders of the upper gastrointestinal tract. This person would also be licensed and board certified in gastroenterology.

21. I have also been informed that claim language should be interpreted in a way a person of ordinary skill would understand that language. I understand that the claim construction process begins with an assessment of the ordinary meaning of the words of the claim. In addition, I have been informed that the specifications and file histories of the '504 and '192 patents, including the prior art references submitted to or considered by the patent office, should be considered to better understand the claims. I have reviewed the file histories of the '504 and '192 patents.

22. Counsel has asked me to comment on how a person of ordinary skill in the art would understand certain claim language used in the claims of the '504 and '192 patents.

B. '504 Patent Claim Language

1. “administration [of/to]”

a. Ordinary meaning

23. The language “administration of” appears in claim 6 and the language “administration to” appear in claims 7 of the '504 patent.

24. A person of ordinary skill would understand the terms “administration of” and “administration to” as referring to the means by which a treatment is delivered to a patient. For example, a drug may be administered as an oral tablet or pill, oral liquid, anal suppository, transdermal patch, intranasal spray, injection (*e.g.*, parenteral, subcutaneous, intravenous) and various other suitable means. In each case, administration refers to a means employed to deliver the intended medication to the target patient in an effective manner.

25. I understand that Hanmi has proposed that “administration” of/to should be construed as requiring “the prescription by a physician or other licensed healthcare professional, dispensing and ingestion.”

26. While administration of a drug *may* involve healthcare professionals (*e.g.*, prescription by a physician, dispensing by a physician or pharmacist or injection of a medicine to a patient) it is certainly not so limited. For example, omeprazole is itself one of many examples of a drug that may be obtained over-the-counter (as Prilosec® OTC) and administered orally without a prescription or involvement of a healthcare professional. The language “administration of” or “administration to” applies equally well to OTC omeprazole as it would to a physician-prescribed, physician-dispensed and would be understood the same by a person of ordinary skill. This common meaning of “administration”—well understood by persons of ordinary skill—would be illogical under Hanmi’s construction.

b. The '504 patent specification and prosecution history

27. The term “administration” is used throughout the '504 patent specification in a manner consistent with the ordinary meaning discussed above.

28. Throughout the '504 patent specification “administration” is always used in the context of describing a means by which a treatment is delivered. The specification describes a number of these means, including “pharmaceutical formulations for oral, rectal, parenteral or other modes of administration.” Col. 5, lines 12-15.

29. In each of the claims in the '504 patent where the term “administration” appears, that term is always modified by the term “oral,” indicating that as used in the '504 patent, “administration” refers to the means of delivery of the medicine (*i.e.*, by mouth). Claims 1, 6-7 and 8-9.

30. The '504 patent specification also describes various pharmaceutical formulations and preparations to facilitate and/or improve the administration of esomeprazole via oral, rectal, and parenteral routes (*e.g.*, “[i]n the preparation of a pharmaceutical formulations in form of dosage units for oral administration the optically pure compound may be mixed with solid, powered carrier...”; “[d]osage units for rectal administration may be prepared in the form of suppositories...”; “[l]iquid preparation for oral administration may be prepared in the form of syrups or suspensions...”; “[s]olutions for parenteral administrations may be prepared... in pharmaceutically acceptable solvents...” Col. 5, line 12 to col. 6, line 25.

31. The use of “administration of” or “administration to” as a means of delivery of medicine in the '504 patent is further confirmed by the explicit description of “route of administration”. Col. 6, lines 21-24.

32. I cannot identify any portion of the '504 patent specification that would limit “administration” to a prescription or the involvement of any “licensed healthcare professional.”

33. Furthermore, the use of the word “patients” in the ’504 patent does not necessarily *require* the participation of a physician or healthcare professional. Col. 2, lines 12-37 and col. 6, lines 21-25 *cited* by Hanmi.

34. “Patients” as described in the sections cited by Hanmi, indicates nothing more than a person with a condition that may benefit from treatment. For example, the specification states that the claimed compounds may be used “in patients on NSAID therapy.” Non-steroidal anti-inflammatory drugs (NSAIDs) are common drugs used for pain relief and include many over the counter medications like aspirin, ibuprofen and naproxen. Thus, “patients on NSAID therapy” is not limited to patients under the supervision of a healthcare professional.

35. “Patients” as used in the ’504 patent, does not necessarily indicate or suggest that the participation of a physician or other healthcare professional is required. And, nowhere does the ’504 patent specification or its file history limit treatment of a “patient” to require the involvement of a healthcare professional.

36. “Administration” as used in the ’504 patent is entirely consistent with the ordinary meaning of the term discussed above.

2. “a mammal including man in need of such treatment”

a. Ordinary meaning

37. The language “a mammal including man in need of such treatment” appears in claim 7 of the ’504 patent.

38. I understand that Hanmi asserts that this term should be construed as requiring that the need for treatment of a “gastrointestinal inflammatory disease [be] recognized and/or appreciated by the physician or other healthcare professional.”

39. The meaning of the first part of the language, “a mammal including man”, is clear: it refers to humans.

40. With respect to the remainder of the claim language “in need of such treatment,” a person of ordinary skill would understand this term to mean a person with a condition who may benefit from treatment—in other words, it refers to a class of patient or limits humans to a particular class or group (*e.g.*, persons with a gastrointestinal inflammatory disease). While the “need” for a medical treatment may be assessed by a physician, as noted above, many drugs may be obtained over-the-counter and administered without a prescription or involvement of any “licensed healthcare professional.”

41. The term does not require recognition or appreciation by anyone, let alone a healthcare professional.

b. The '504 patent specification and prosecution history

42. Nowhere does the specification limit claim 7, “[a] method for the treatment of gastrointestinal inflammatory disease comprising the oral administration to a mammal including man in need of such treatment of a pharmaceutical formulation”, to require recognition or appreciation by a healthcare professional or anyone else.

43. Nothing in the claims, specification or prosecution history would indicate to a person of ordinary skill in the art that the language “in need of such treatment” in claim 7 refers to anything other than a class of people with a condition (*i.e.*, gastrointestinal inflammatory disease) that may benefit from the administration of the claimed composition.

44. A person “in need of such treatment” as used in the ’504 patent is entirely consistent with the ordinary meaning such language would have to a person of ordinary skill in the art.

C. ’192 Patent Claim Language

1. “administering to a mammal in need of treatment”

a. Ordinary meaning

45. The term “administering to a mammal in need of treatment” appears in asserted claims 1–7, 10, 11 and 23 of the ’192 patent.

46. For the same reasons delineated while discussing the terms “administration [of/to]” as used in the ’504 patent (paragraphs 23-27 above), and “a mammal including man in need of such treatment” as used in the ’504 patent (paragraphs 37-41 above), a person of ordinary skill would understand the term “administering to an a mammal in need of treatment” as the suitable means by which a drug or therapy is delivered to a person with a condition who may obtain a benefit from treatment with that drug or therapy. In my opinion, a person of ordinary skill in the art would understand “administering” to refer to the means of delivery and “mammal in need of treatment” as language that limits the patient class.

47. I understand that Hanmi asserts that this term should be construed to mean “the prescription by a physician or other licensed healthcare professional, dispensing and delivery by any suitable means.”

48. Again, administration of a drug *may* involve healthcare professionals (*e.g.*, prescription by a physician, dispensing by a physician or pharmacist or injection of a medicine to a patient), and the “need” of treatment *may* be assessed by a healthcare professional, but neither term is so limited. As noted above, omeprazole is just one of numerous examples of drugs that

may be obtained over-the-counter (as Prilosec® OTC) and administered orally without a prescription or involvement of a healthcare professional.

49. The term “administering to a mammal in need of treatment” does not require recognition or appreciation by anyone, including a healthcare professional.

b. The ’192 patent specification and prosecution history

50. The ’192 patent specification uses “administering” to refer to the means by which the compounds of the invention may be delivered. For example, dependent claims 7, 8 and 9 limit independent method claims 1 and 2 to those in which the compound is “administered orally”, “administered parenterally” or “administered by intravenous infusion”. Similarly, claims 19 and 20, which depends from claim 12, limits the method to those in which the “medicament” is produced for “oral administration” or “administered parenterally”.

51. The specification further supports this understanding, explaining that “[a]ny suitable route of administration may be employed for providing the patient with an effective dosage of [esomeprazole].” Col. 4, lines 3-5. Including for example, “oral, parenteral, subcutaneous, intramuscular, rectal, transdermal and the like.” Col. 4, lines 5-8 and lines 19-21.

52. Nowhere do the claims or the specification indicate that a “licensed healthcare professional” *must* be involved either for assessing “need” of a patient or for “administration,” and such a limitation would be inconsistent with the usage of “administration” in reference to the means of delivery in the patent.

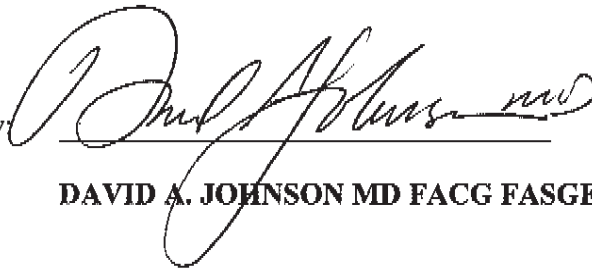
53. "Administering to a [person] in need of treatment" as used in the '192 patent is entirely consistent with the ordinary meaning of the term as it would be understood by a person of ordinary skill in the art.

* * *

54. I declare under penalty of perjury under the laws of the United States of America that the foregoing is true and correct.

Dated: November 7, 2011

By

A handwritten signature in cursive script, appearing to read "David A. Johnson MD", written over a horizontal line.

DAVID A. JOHNSON MD FACG FASGE